IN THE CLAIMS:

Summary of Current Amendments:

Please amend Claims 1-4, 8, and 9, without prejudice to or disclaimer of the subject matter therein.

Listing of Claims:

1. (Currently Amended) A method of structure-based identification of candidate compounds for binding to complement receptor type 2 (CR2) proteins or to a complex of CR2 and its ligand, comprising:

a. providing a three dimensional structure of a CR2 short consensus repeat (SCR) 1-2 region selected from the group consisting of:

i. a structure defined by atomic coordinates of a three dimensional structure of a crystalline CR2 SCR1-2 region in complex with C3d;

ii. a structure defined by atomic coordinates selected from the group consisting of:

(1) atomic coordinates represented in a table selected from the group consisting of Table 2 (CR2-C3d) and Table 3 (CR2 only); and,

(2) atomic coordinates that define a three dimensional structure, wherein at least 50% of said structure has an average root-mean-square deviation (RMSD) from backbone atoms in secondary structure elements in at least one domain of a three dimensional structure represented by said atomic coordinates of (1) of equal to or less than about 1.0Å; and

iii. a structure defined by atomic coordinates derived from CR2 protein molecules arranged in a crystalline manner in a space group R32 so as to form a unit cell of dimensions a=b=170.5Å, c=173.8 Å; ~~and,~~

b. identifying a candidate compound for binding to said CR2 SCR 1-2 region by performing structure based drug design with said structure of (a);

c. synthesizing said candidate compound identified in step (b); and

d. selecting candidate compounds from step (c) that bind to CR2.

2. (Currently Amended) The method of Claim 1, wherein said step of ~~identifying~~ selecting comprises selecting candidate compounds that bind to and activate CR2.

3. (Currently Amended) The method of Claim 1, wherein said method further comprises:

~~c.~~ e. selecting candidate compounds ~~of (b)~~ that inhibit the binding of CR2 to its ligand.

4. (Currently Amended) The method of Claim 3, wherein said step ~~(c)~~ (e) of selecting comprises:

i. ~~producing said candidate compound identified in step (b);~~

~~ii.~~ contacting said candidate compound ~~identified in step (b)~~ synthesized in step (c) with CR2 or a fragment thereof and a CR2 ligand or a fragment thereof under conditions in which a CR2-CR2 ligand complex can form in the absence of said candidate compound; and

~~iii.~~ ii. measuring the binding affinity of said CR2 or fragment thereof to said CR2 ligand or fragment thereof; wherein a candidate inhibitor compound is selected as a compound that inhibits the binding of CR2 to its ligand when there is a decrease in the binding affinity of said CR2 or fragment thereof for said CR2 ligand or fragment thereof, as compared to in the absence of said candidate inhibitor compound.

5. (Original) The method of Claim 3, wherein said ligand is selected from the group consisting of C3d, CD23, and Epstein Barr Virus (EBV) gp350/220, or CR2-binding fragments thereof.

6. (Original) The method of Claim 3, wherein said ligand is a gp350/220 viral membrane protein from EBV or a CR2-binding fragment thereof.

7. (Original) The method of Claim 3, wherein said CR2 protein or fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

8. (Currently Amended) The method of Claim 1, wherein said method further comprises:

~~c.~~ e. selecting candidate compounds that stabilizes a complex of CR2 with its ligand.

9. (Currently Amended) The method of Claim 8, wherein step ~~(c)~~ (e) of selecting comprises:

i. contacting said candidate compound ~~identified in step (b)~~ synthesized in step (c) with a CR2-CR2 ligand complex, wherein said CR2-CR2 ligand complex comprises CR2 or a fragment thereof and a CR2 ligand, or a fragment thereof;

ii. measuring the stability of said CR2-CR2 ligand complex of (i), wherein a candidate stabilizer compound is selected as a compound that stabilizes the CR2-CR2 ligand complex when there is an increase in the stability of the said complex as compared to in the absence of said candidate stabilizer compound.

10. (Withdrawn) The method of Claim 8, wherein said ligand is selected from the group consisting of C3d and CD23.

11. (Withdrawn) The method of Claim 8, wherein said CR2 protein or fragment thereof comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

12. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the SCR2 domain of said CR2.

13. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the interface between the SCR1 and SCR2 domains of CR2.

14. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the dimer interface between two CR2 proteins.

15. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the interface between CR2 and C3d, C3, a CR2-binding fragment of C3 containing C3d, or a fragment thereof.

16. (Original) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the B strand and the B-C loop of CR2 SCR2 comprising the segment: G79-G80-Y81-K82-I83-R84-G85-S86-T87-P88-Y89.

17. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a site on the B strand of CR2 SCR2 comprising position K100.

18. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a segment of CR2 SCR2 comprising V130-F131-P132-L133.

19. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to a segment of CR2 SCR2 comprising the fragment T101-N102-F103.

20. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to the loop between helix 2-3 of C3d comprising the segment Q68-P69-S70-S71.

21. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to Helix 5 of C3d comprising the segment S104-Q105-V106-L107-C108-G109-A110-V111-K112-W113-L114-I115-L116-E117-K118-Q119-K120-P121-D122.

22. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to Helix 7of C3d comprising the segment N170-S171-L172-P173-G174-S175-I176-T177-K178-A179-G180-D181-F182-L183-E184-A185.

23. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises identifying candidate compounds for binding to amino acid residues at positions

84 and 86 of an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

24. (Original) The method of Claim 1, wherein said step of identifying comprises directed drug design.

25. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises random drug design.

26. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises grid-based drug design.

27. (Withdrawn) The method of Claim 1, wherein said step of identifying comprises computational screening of one or more databases of chemical compounds.

28-47. (Cancelled)

REMARKS

Telephone Interview

Applicants would like to thank Examiner Zhou and Examiner Brusca for the courtesy extended to Applicants' representatives: Angela Dallas Sebor (agent of record), Annalissa Philbin (counsel for Assignee, Michael Holers (inventor) and Xiaojiang Chen (inventor), during the telephone interview of October 9, 2003, during which the rejections under 35 U.S.C. § 103 were discussed. At the beginning of the interview, Examiner Zhou informed Applicants' representatives that upon further consideration of the arguments presented in the last filed response, the rejection of Claims 1-7 and 24 under 35 U.S.C. § 103 over of Mond et al. in view of Prodinger et al. and further in view of Hampton Research will be withdrawn. Applicants agent then presented and reiterated argument against the rejection of Claims 1-7, 16 and 24 under 35 U.S.C. § 103 over Mohammadi et al. The Examiners suggested that the addition of further a "wet chemistry" step to the method of Claim 1, wherein the candidate compound identified by the method of drug design is further synthesized for testing, would overcome the rejection. In order to expedite prosecution, Applicants have adopted the Examiner's suggestion with regard to the addition of "wet chemistry steps". The claims are believed to be in a condition for allowance or at a minimum, in a better condition for appeal.

Claim Amendments

Claim 1 has been amended to add a step (c) of synthesizing the candidate compound identified in step (b) and a step of selecting compounds from step (c) that bind to CR2. Support for these amendments is found in original Claim 2 and in the specification on page 10, lines 26-27; page 27, lines 5-9; and page 35, line 4 to page 41, line 11, for example. The remaining amendments are made so that the dependent claims are consistent with the amendment to Claim 1. These amendments add no new matter, and will not require any additional search on the part of the Examiner, given the subject matter of original dependent Claims 2-11, and therefore the Examiner is respectfully requested to enter the amendments.

Non-elected Species

Claims directed to non-elected species are still pending in anticipation of allowance of a generic claim. It is submitted that the generic Claim 1 is in a condition for allowance and Applicants again assert that the invention is not limited to the elected species.

Drawings

Applicants acknowledge the acceptance of the formal drawings for the application. A Petition to Accept Color Drawings with the requisite fee was filed with the first submission of formal drawings on July 26, 2001. The specification has been amended in this response to add the requisite statement to the specification.

Rejection of Claims 1-7 and 24 Under 35 U.S.C. § 103:

The Examiner has rejected Claims 1-7 and 24 under 35 U.S.C. § 103, contending that these claims are unpatentable over Mond et al. in view of Prodinger et al. and in further view of Hampton Research, for the reasons of record.

Applicants respectfully traverse the rejection of Claims 1-7 and 24 under 35 U.S.C. § 103 for the reasons set forth in the last filed response. During the October 7 telephone interview, the Examiners informed Applicants' agent that the prior arguments were, upon further consideration, persuasive, and that this rejection would be withdrawn.

In view of the foregoing remarks, Applicants request that the Examiner withdraw the rejection of Claims 1-7 and 24 under 35 U.S.C. § 103.

Rejection of Claims 1-7, 16 and 24 Under 35 U.S.C. § 103:

The Examiner has rejected Claims 1-7, 16 and 24 under 35 U.S.C. § 103, contending that these claims are unpatentable over Mohammadi et al. for the reasons of record.

Applicants respectfully traverse the rejection of Claims 1-7, 16 and 24 under 35 U.S.C. § 103, for the reasons of record. Further, as discussed in the October 7 telephone interview, Applicants believe that the Examiner's use of *In re Gulack* is misplaced, particularly since in that case, the holding that the material in question was not functionally related to the substrate of the claims was

reversed. Applicants strongly maintain the position that the rejection on the basis of obviousness is improper, since the present rejection can only be maintained if the Examiner dissects the claim, excises the material in question, and declares the remaining portion of the mutilated claim to be unpatentable. This is clearly an improper application of 35 U.S.C. § 103, which requires that the claim be read as a whole.

In any event, Applicants wish to expedite prosecution and therefore have adopted the Examiners' suggestion to add steps to the method that require the synthesis of candidate compounds identified by the method of structure-based design for further testing in a "wet chemistry" process. Support for this amendment has been discussed above. Clearly, Mohammadi et al. does not teach or suggest a method whereby a compound that is predicted to bind to CR2 is synthesized and in which compounds that actually bind to CR2 are selected.

In view of the foregoing discussion, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-7, 16 and 24 under 35 U.S.C. § 103.

Applicants have attempted to respond to all of the Examiner's concerns as set forth in the May 30 Office Action and submit that the claims are in a condition for allowance. In the event that the Examiner has additional concerns regarding the claims, he is encouraged to contact the below-named agent at (303) 863-9700 to expedite prosecution.

Respectfully submitted,

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